



# **Armed Forces College of Medicine AFCM**



# **Lipoprotein Metabolism 1**

**Dr. Manal Basyouni**  
**Professor of Medical Biochemistry  
& Molecular Biology**

# INTENDED LEARNING OBJECTIVES (ILO)



**By the end of this lecture the student will be able to:**

1. Discuss the structure, different types, origin and methods of lipoproteins separation.
2. List functions of lipoproteins
3. Outline the role of different apolipoproteins.
4. Explain metabolism of chylomicrons.

# Case scenario



- A 65 -year-old man complained of **pain in the left side of the chest** radiating to the left arm on doing any effort.
- He was **hypertensive** and heavy smoker. He consulted a cardiologist who recommended doing ECG and lipid profile.
- **Lipid profile was** : TAG 250 mg % (Normal Less than 150 mg/dL) , Cholesterol 300 mg% (N Less than 200 mg/dL) , LDL 180 mg % (N Less than 100 mg/dL), HDL 30mg % (N high than 50 mg/dL) .

# Case discussion



**What are the patients complaints?**

Pain in the left  
side of the  
chest

**What are the risk factors in this patient?**

Heavy  
smoking

Hypertension

**What did the investigations reveal?**

High  
TAG

High  
Choleste  
rol

High LDL

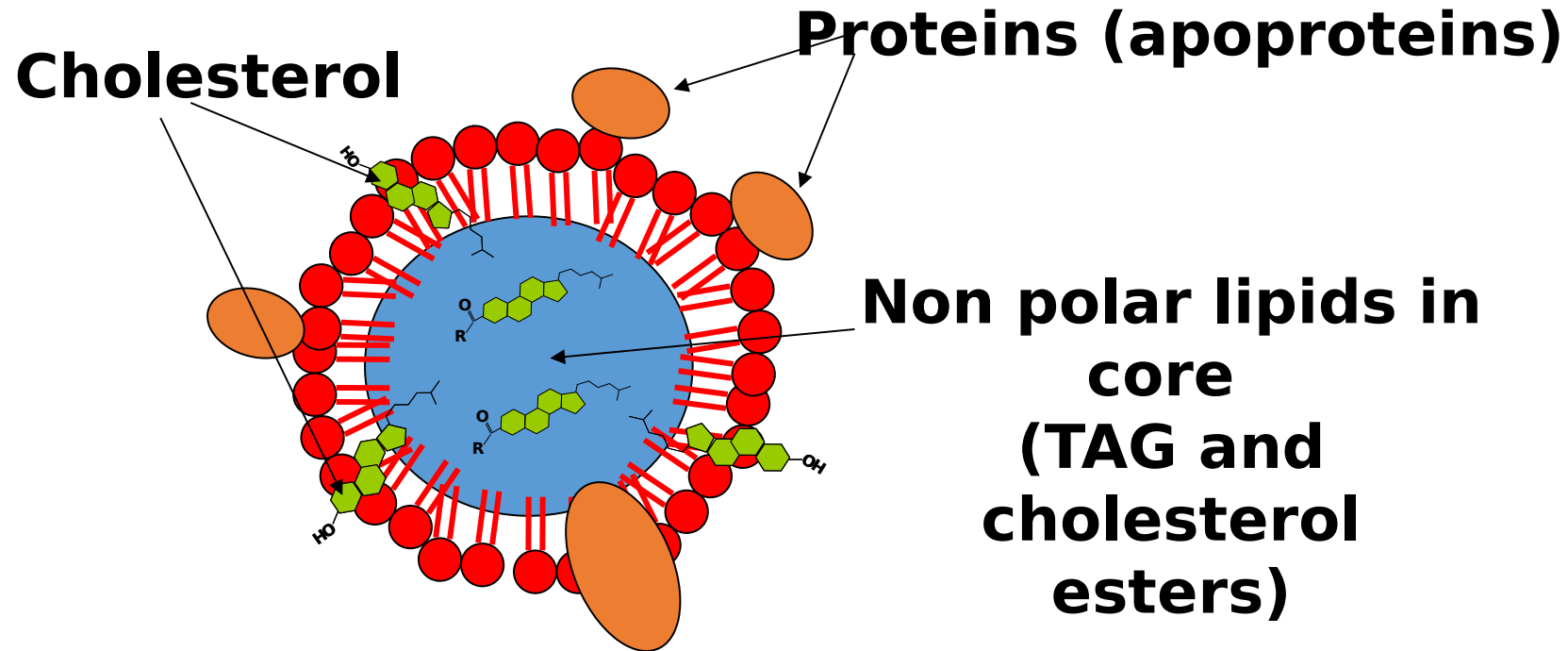
Low HDL

# Biochemical Discussion



- **What is LDL and HDL?**
- **What is the relation between impaired lipid profile and angina pain?**

# Lipid transport in the circulation



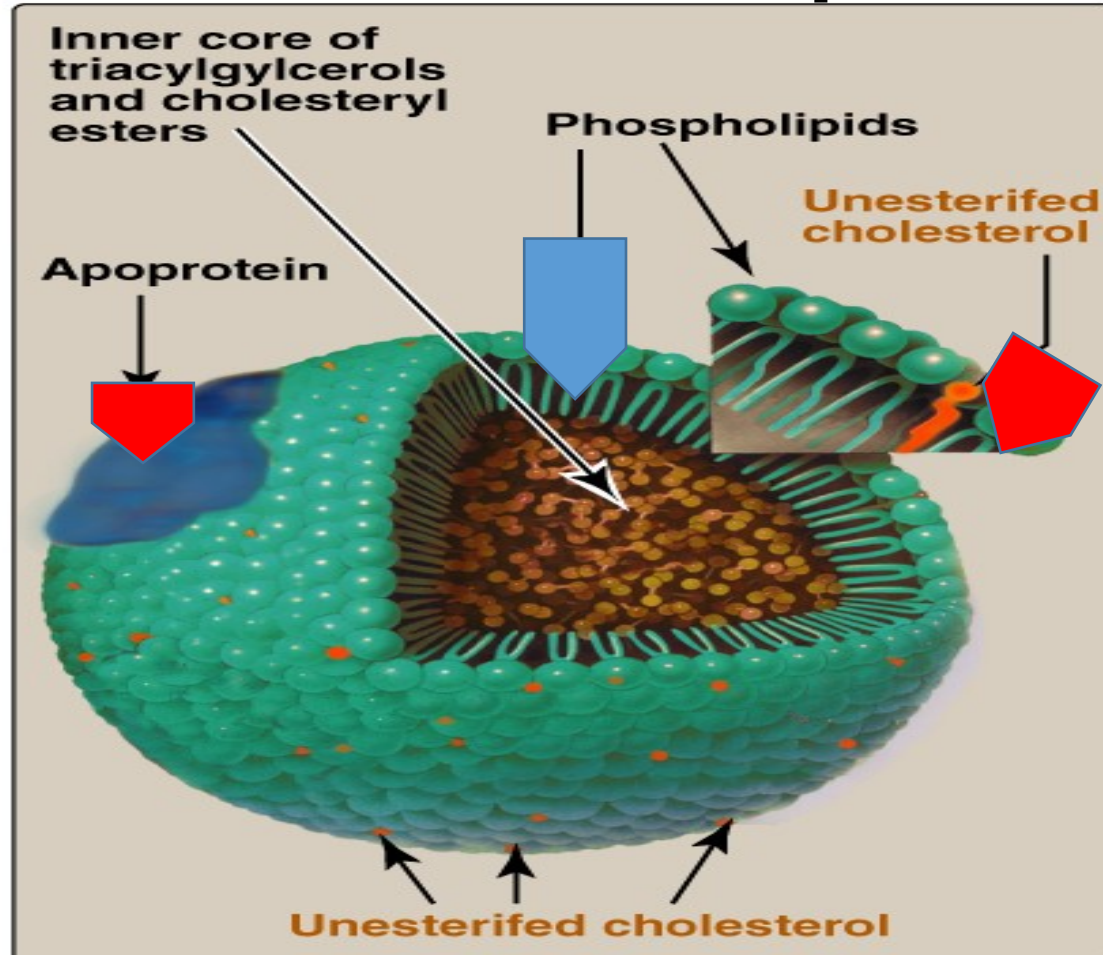
**Lipids are insoluble in plasma. In order to be transported they are combined with specific proteins to form**

**lipoproteins**

# Lipoprotein Structure



**Spherical molecules of lipids and proteins (apoproteins)**



**Outer coat:**

**-Amphipathic lipids:**

**Phospholipids  
Free  
Cholesterol**

**+**

**-Apoproteins**

**Inner core:**

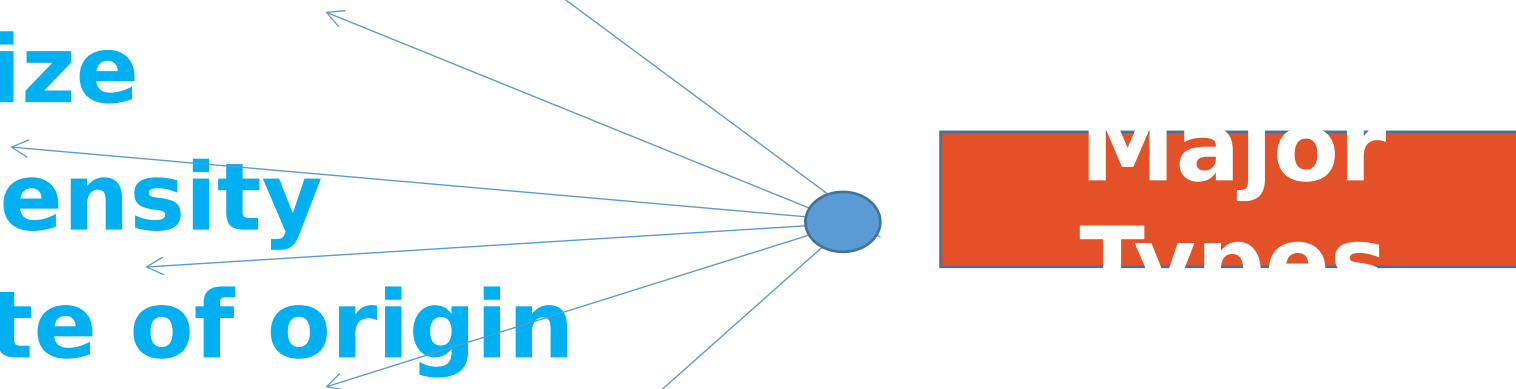
**Hydrophobic  
lipid**

[https://www.google.com.eg/search?biw=1252&bih=600&tbm=isch&sa=1&ei=kqVFXYq2AYGPlwTxmKPgBA&q=Composition+of+Lipoproteins&oeq=Composition+of+Lipoproteins&gs\\_l=img.12..0.94761.94761..96274...0.0..0.133.133.0j1.....0....2j1..gws-wiz-img.LCHviiyioxZU&ved=0ahUKEwiKx53NCardio-pulmonary ModulebjAhWBx4UKHXHMCEwQ4dUDCAY#imgsrc=IQZx\\_V3ZNf853M:](https://www.google.com.eg/search?biw=1252&bih=600&tbm=isch&sa=1&ei=kqVFXYq2AYGPlwTxmKPgBA&q=Composition+of+Lipoproteins&oeq=Composition+of+Lipoproteins&gs_l=img.12..0.94761.94761..96274...0.0..0.133.133.0j1.....0....2j1..gws-wiz-img.LCHviiyioxZU&ved=0ahUKEwiKx53NCardio-pulmonary ModulebjAhWBx4UKHXHMCEwQ4dUDCAY#imgsrc=IQZx_V3ZNf853M:)



# Why do we have different types of lipoproteins?

- **Specific function**
- **Composition**
- **Size**
- **Density**
- **Site of origin**
- **Type of apolipoprotein.**



**Major  
Types**

# Classification of Lipoproteins



**1-Chylomicrons CM: derived from small intestine and carries exogenous dietary TAG.**

**2-Very low density lipoproteins (VLDL) derived from liver and carries endogenous TAG.**

**3-Low density lipoproteins (LDL):**  
**carries cholesterol from liver to tissues (Bad Lipoprotein).**

**4-High density lipoproteins (HDL):**  
**carries cholesterol from tissues to liver to be excreted in bile (Good Lipoprotein).**



# FOUR MAJOR LIPOPROTEIN CLASSES

|                          | High Density                                                                                                                | Low Density                                                                          | Very Low Density                                                                     | Chylo-microns                                                                        |
|--------------------------|-----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| <b>Apolipo-proteins</b>  | A-I, A-II<br>E, Cs                                                                                                          | B-100                                                                                | B-100, Cs,<br>E                                                                      | B-48, Cs, E,<br>A-I, A-II                                                            |
| <b>Major core lipids</b> | Cholesteryl ester                                                                                                           | Cholesteryl ester                                                                    | Triglyceride                                                                         | Triglyceride                                                                         |
| <b>Relative sizes</b>    | <br>HDL <sub>2</sub><br>HDL <sub>3</sub> |  |  |  |

# Separation of lipoproteins

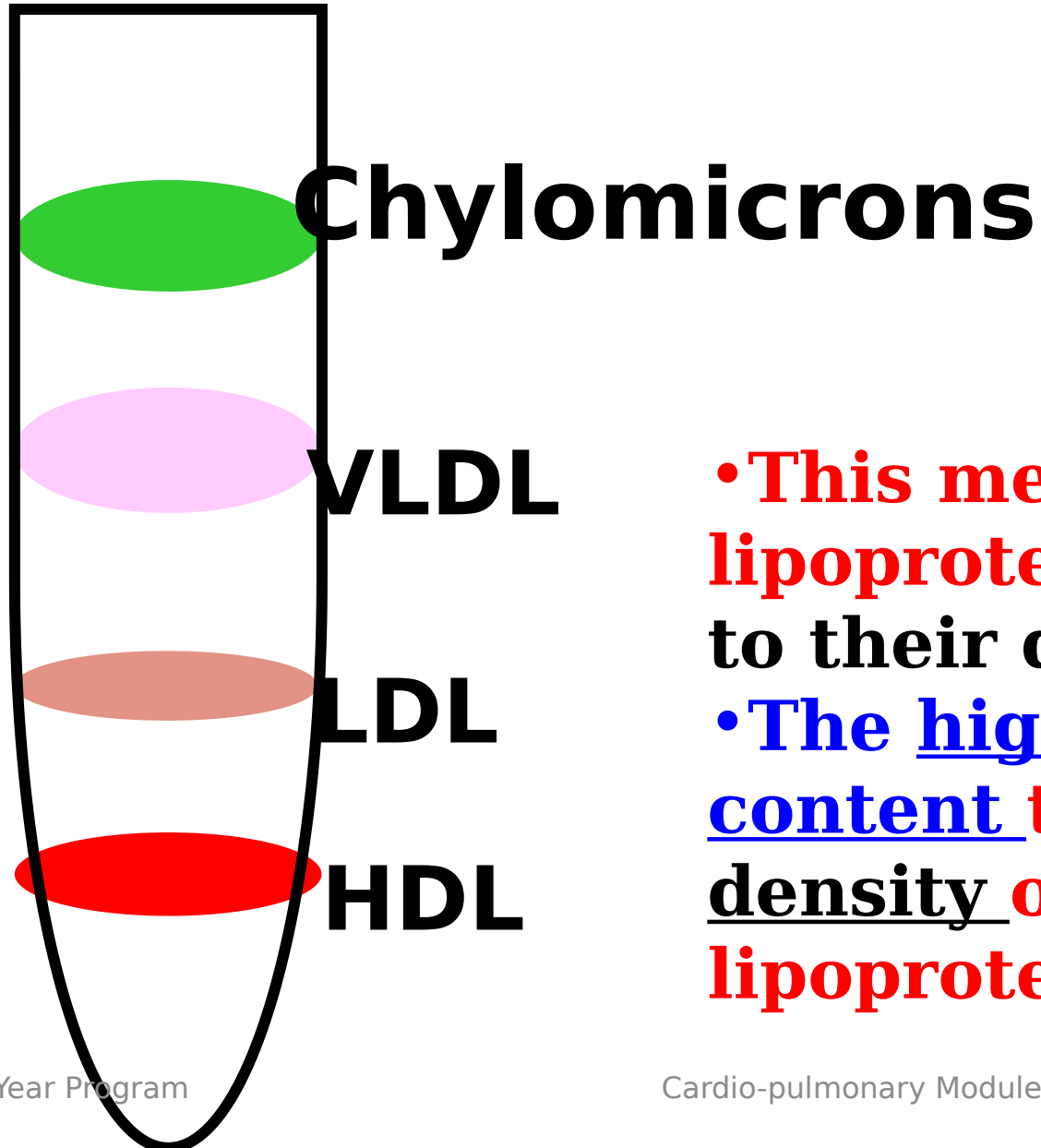
## By 2 methods :



**1-  
Ultracentrifugation**

**2- Electrophoresis**

# Ultracentrifugation

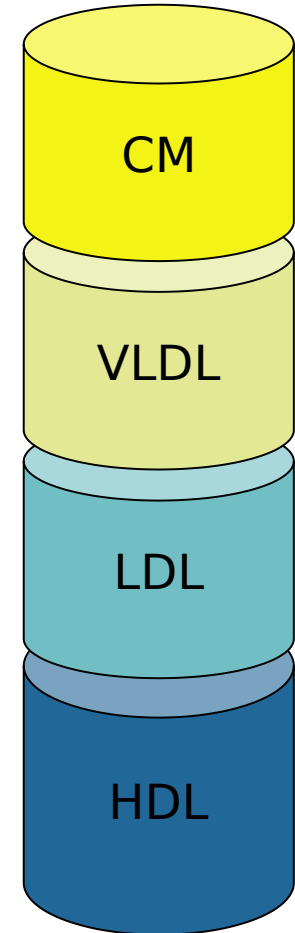
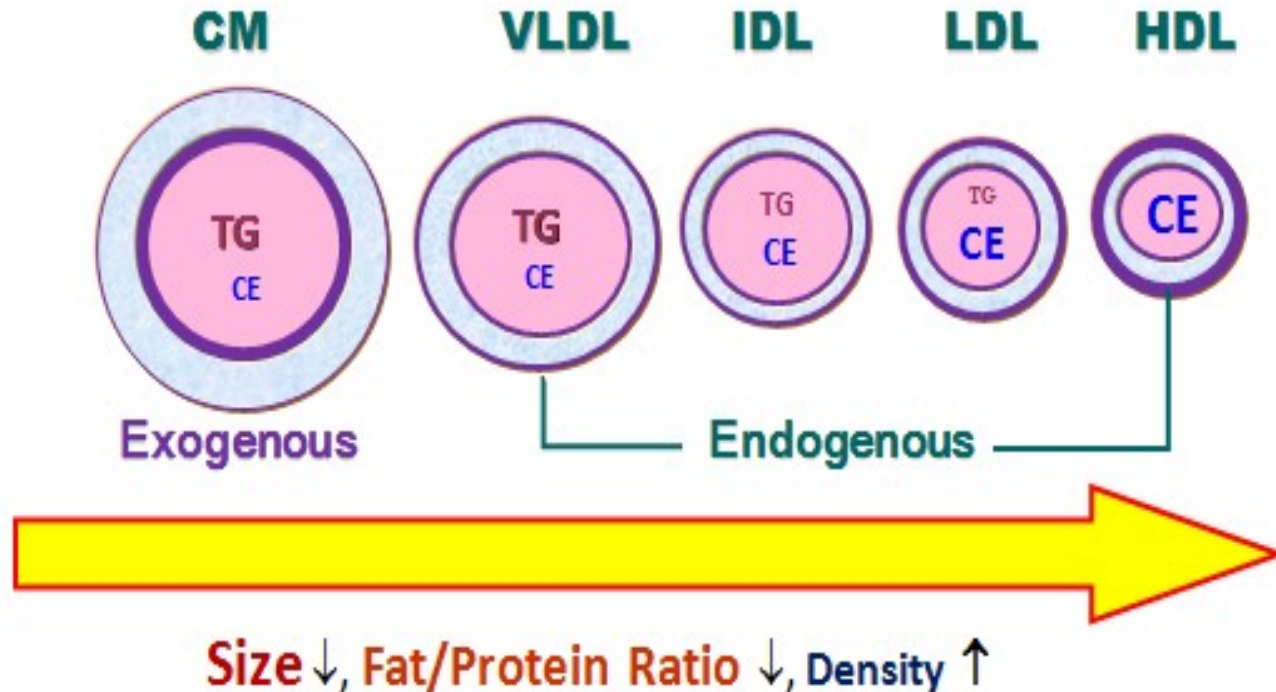


- **This method separates lipoproteins according to their density.**

- **The higher the fat content the lower the density of the lipoprotein particle.**

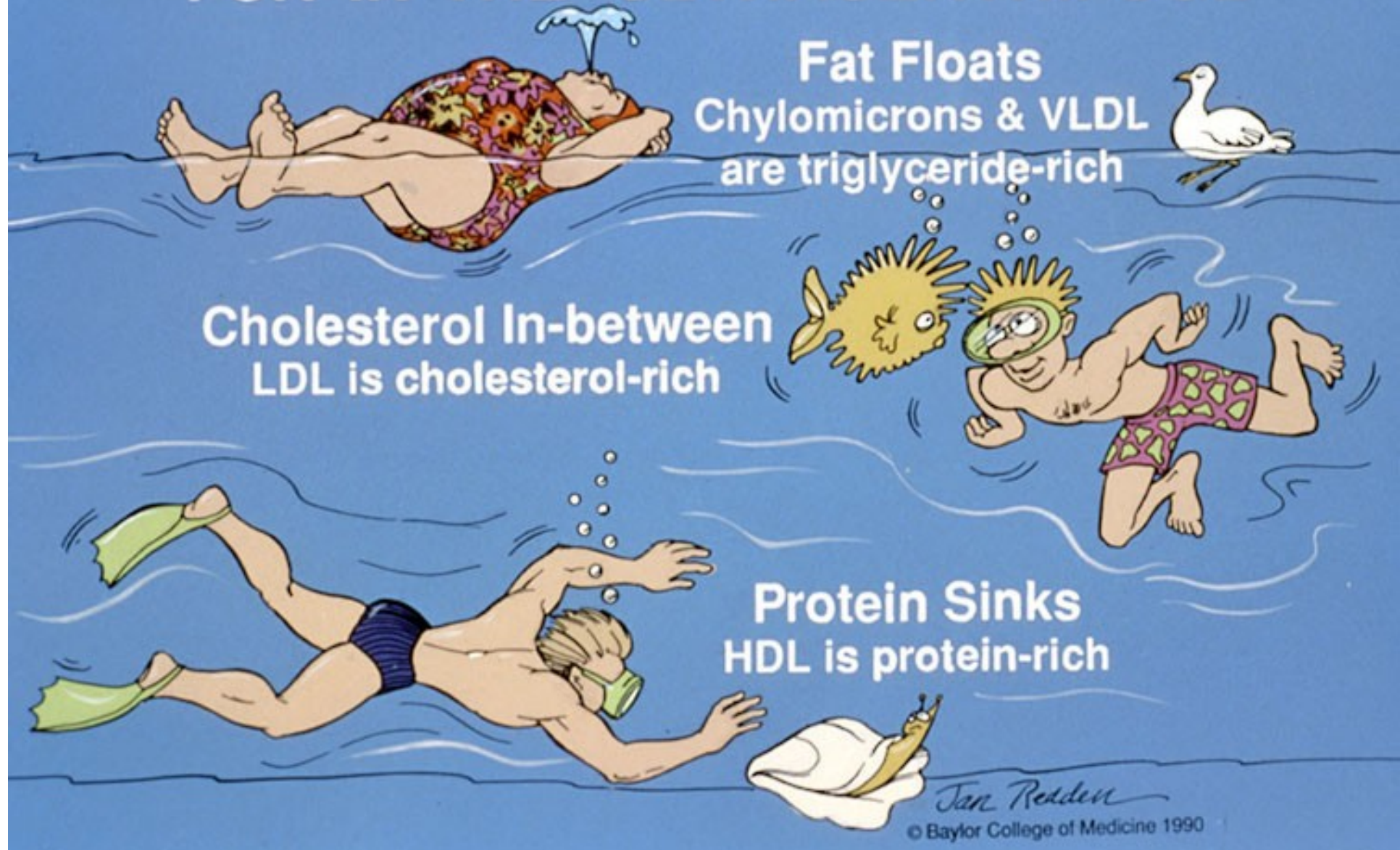
## Ultracentrifugation

- Depending on densities\_
- Fat is less dense than water
- As lipid content is increased, density is decreased





# FUN IN THE ULTRACENTRIFUGE





# Electrophoresis



- **Movement of lipoproteins in an electric field is depending on the charges located on their proteins.**
- **Higher protein content (negatively charged) moves faster towards the anode.**

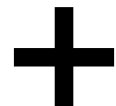
**Chylomicrons**

**—  
origin**

**Beta (LDL)**

**Pre  $\beta$  (VLDL)**

**Alpha (HDL)**



# Functions of lipoproteins



## 1- Transport of triacylglycerol (TAG rich particles)

**Chylomicrons: transport TAG of dietary origin.**

**VLDL: transport TAG of endogenous hepatic origin.**

## 2- Transport of cholesterol (cholesterol rich particles )

**LDL: Carries cholesterol from liver to extra-hepatic tissues.**

**HDL: Carries cholesterol from peripheral tissues to liver.**

# Apolipoproteins



**It is the protein part of lipoprotein.  
Five major classes A....to....E with subclasses**

## **Integral proteins Apo B**

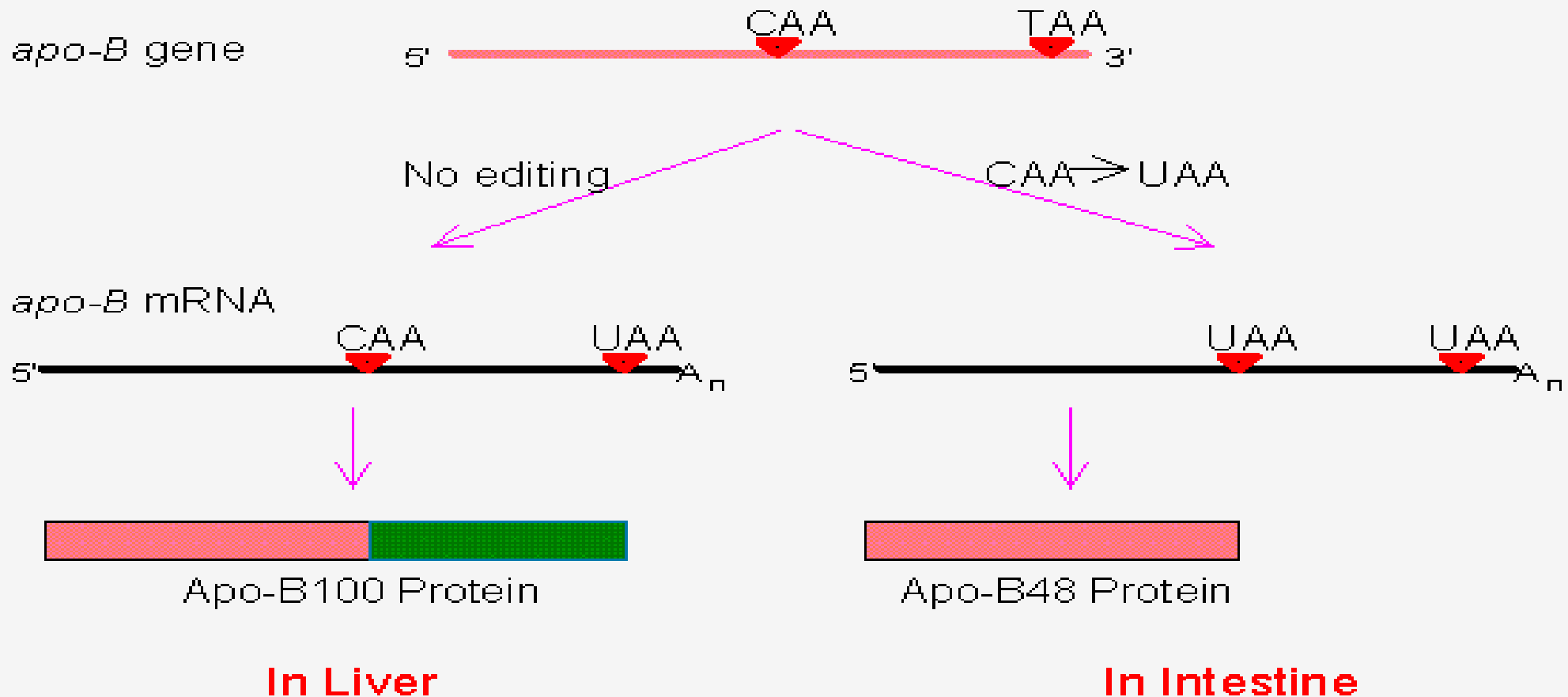
- Apo B-48 (small intestine), Apo B-100 (liver)

## **Peripheral Apo Proteins**

- Apo A I, II, IV
- Apo C I, II, III
- Apo D
- Apo E

# Apo B 100 Vs B48

RNA editing is a molecular process in which the base of a RNA molecule is altered by specific enzymes. In the following example, Cytosine (C) is changed to Uracil (U).



# Functions of Apolipoproteins



## 1- Structural

Some are essential **structural components** of the lipoprotein particles, others are **transferred freely** between lipoproteins.

## 2-Regulatory

Activators or coenzymes for enzymes involved in lipoprotein metabolism.

## 3- Ligands

Recognition sites for cell- surface receptors.



**Receptors for chylomicron remnants are specific for :**

**a- Apo A**

**b- Apo B-48**

**c- Apo C**

**d- Apo E**

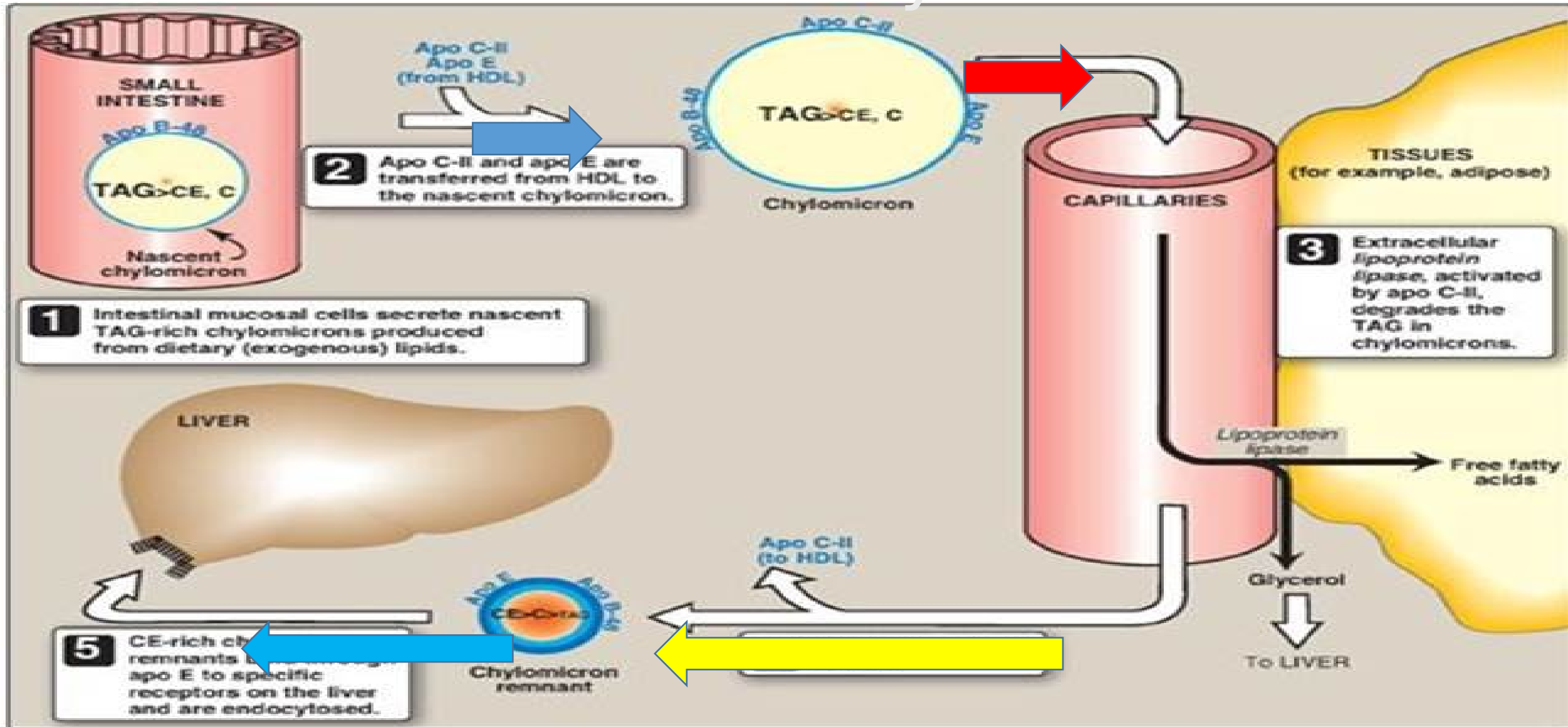
**e- Apo B-100**



# Lipoprotein Metabolism



# Metabolism of Chylomicrons





# Chylomicrons (CM)

- CM are assembled in intestinal mucosal cells , enter the lymphatics then the blood.
- Carry **TAG of (dietary origin)** to peripheral tissues.
- **Nascent CM**: contains Apo B-48 (48% of the protein coded by Apo B gene)
- **Mature CM** : contains Apo B-48 plus **Apo C-II** and **Apo E** ( taken from HDL during circulating in blood )
- CM are responsible for physiological milky appearance of plasma (up to 2 hours after meal).
- **Lipoprotein lipase** is required to degrade **TAG** into free fatty acids and glycerol.

- As CM circulate in blood, 90% of their TAG in the core are degraded by **lipoprotein lipase**, and decrease in size.
- Apo C II ( **but not Apo E**) returns back to HDL.
- The remaining particles are called **CM remnants**, that are rapidly removed from blood by the liver by endocytosis by specific receptors called **chylomicron remnant receptors** that **recognize Apo E protein.**



## CHYLOMICRON METABOLISM

### + Key Pathways

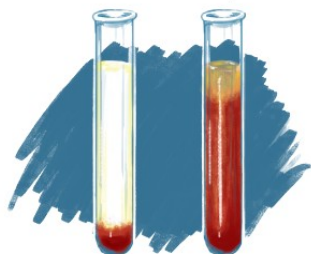
- ✓ Exogenous pathway —
- ✓ Chylomicrons clear dietary lipids.
- ✓ Endogenous pathway —
- ✓ VLDL & LDL transport endogenously synthesized lipids.
- ✓ Reverse cholesterol transport —
- ✓ HDL clears plasma cholesterol

### + Key Enzymes

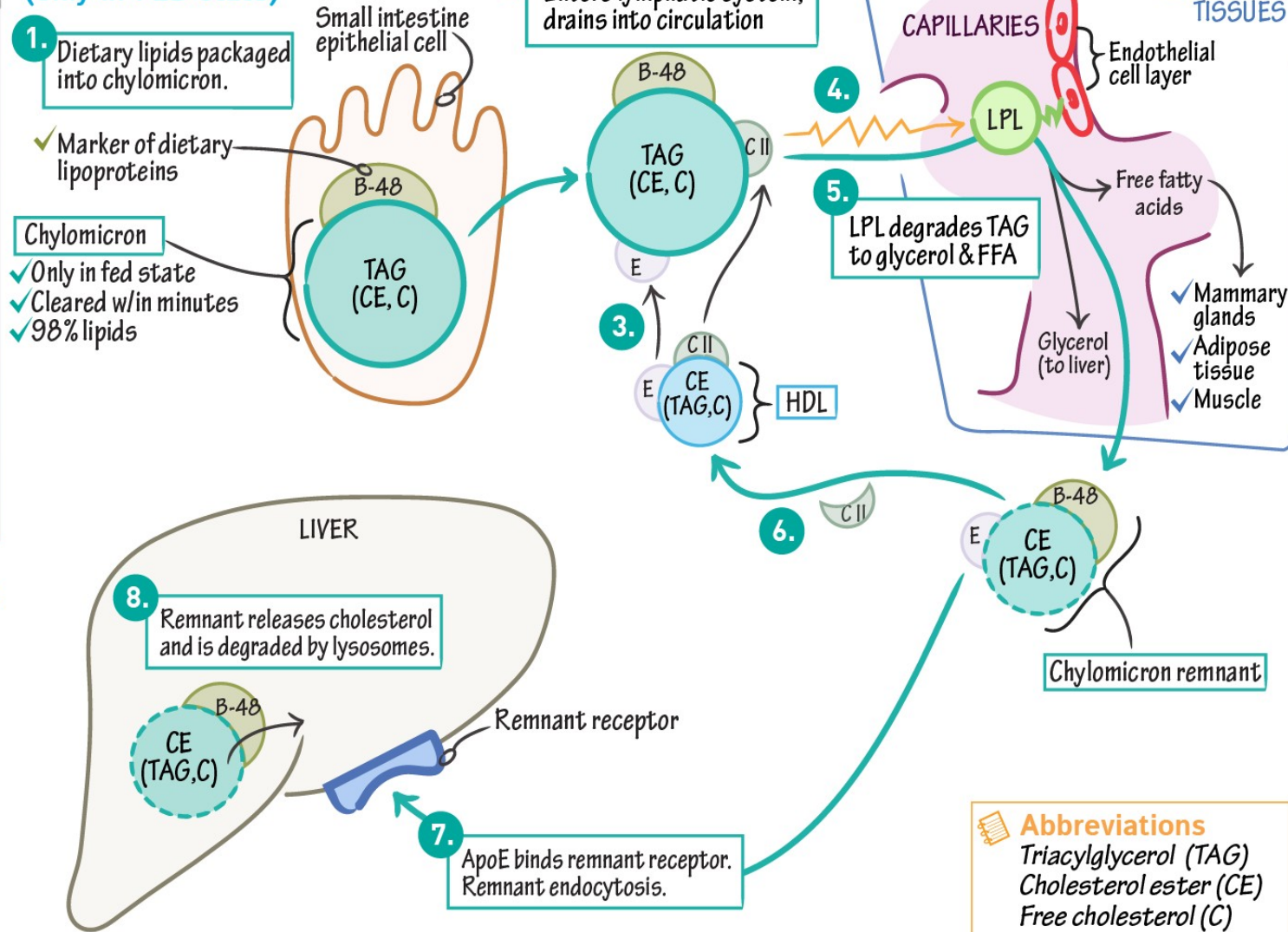
- Degrade triacylglycerol to glycerol and free fatty acids.
- ✓ Lipoprotein lipase —
- ✓ Peripheral capillary endothelial layer
- ✓ Hepatic lipase (also a phospholipase)
- ✓ Hepatic endothelial cells

### § Familial Hyperchylomicronemia

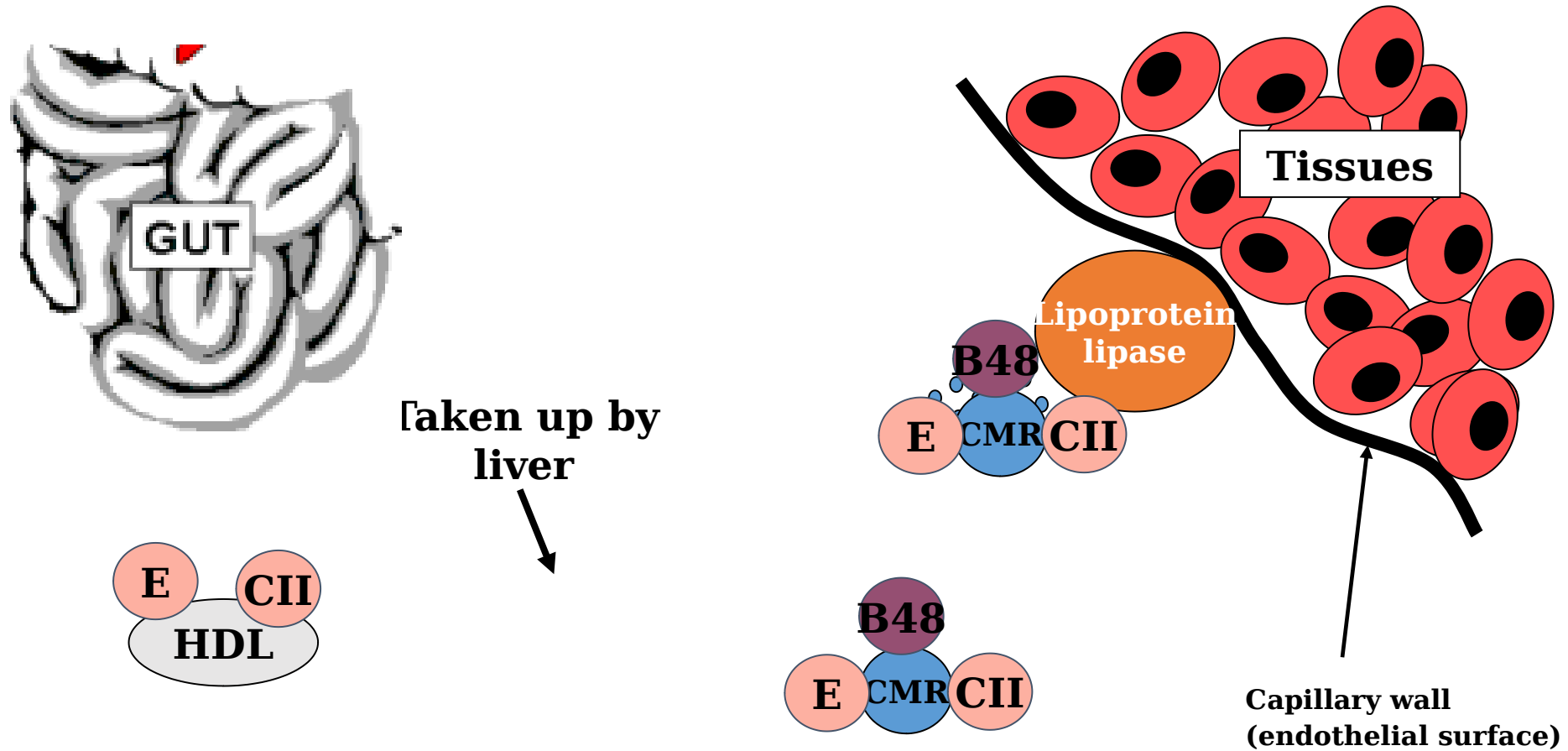
Rare hereditary disease —  
Patients cannot clear chylomicrons.  
Deficiency of LPL or ApoC-II.



### Exogenous Pathway (only in FED state)

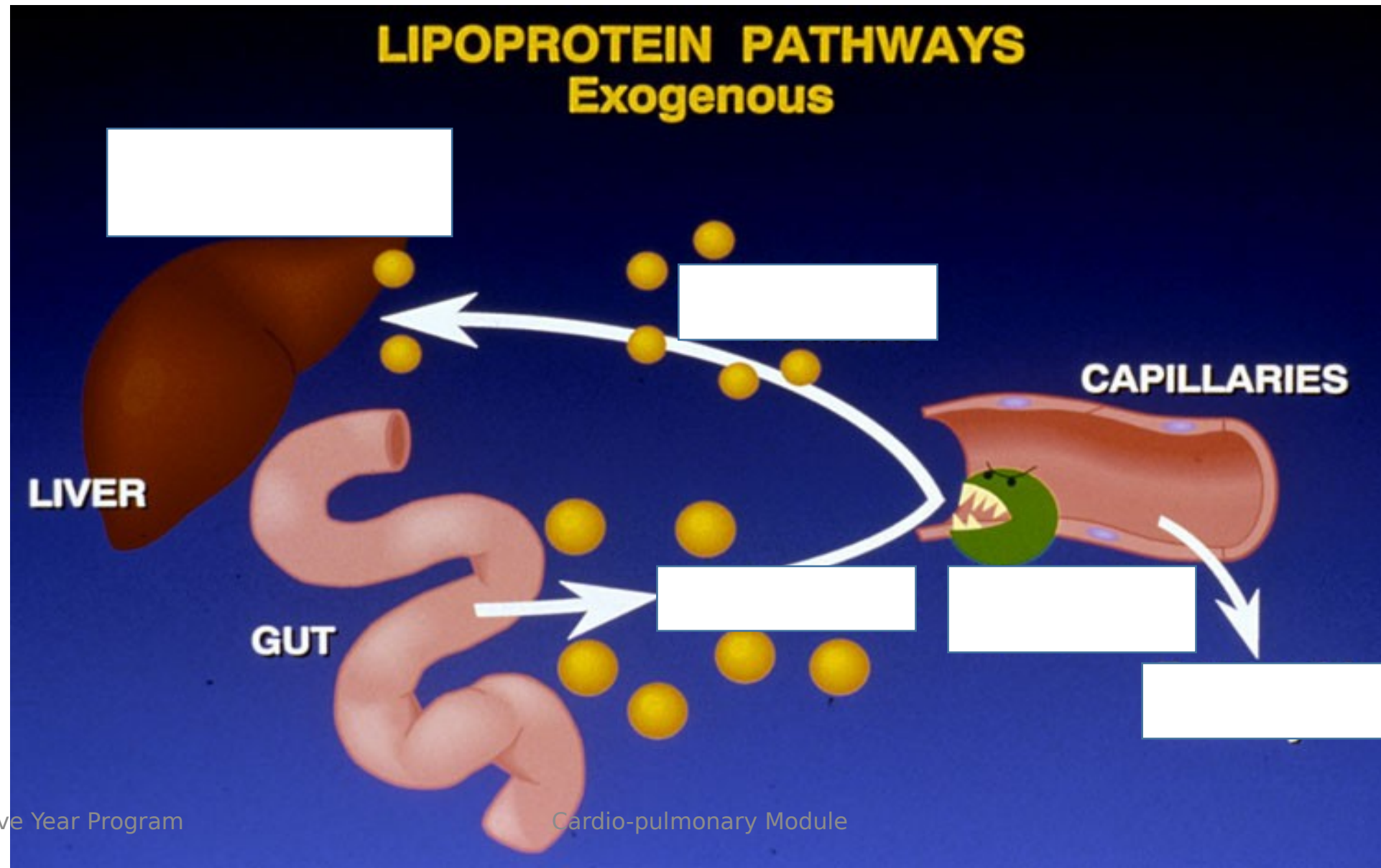


This animation shows how chylomicrons are metabolised once they enter the circulation from the lymphatic system





# Lecture Quiz



**Q: What is the clearing factor?**

- **Lipoprotein lipase**

- **LPL** is synthesized by **adipocytes, cardiac and skeletal muscle** cells, then transferred to be attached by **heparan sulfate** to the capillary wall of most tissues.  
(liver lack this enzyme)





# Lipoprotein lipase (LPL)

- It hydrolyzes **TAG** of CM & VLDL releasing fatty acids and glycerol so it clears plasma from lipoproteins. **FA** are taken up by cells. **Glycerol** is taken by liver.
- **Apo CII** is cofactor activating LPL.
- Insulin enhance LPL synthesis ( Induce synthesis) and activity in adipocytes (this explain why adipose cells gain fat in a well-fed state.)
- It is the only lipase that is induced by **Insulin**





**What is the correct ordering of plasma lipoproteins from the lowest to the greatest density?**

- A- LDL, HDL, VLDL, Chylomicron.**
- B- Chylomicron, VLDL, LDL, HDL.**
- C- VLDL, HDL, LDL, Chylomicron.**
- D- Chylomicron, HDL, VLDL, LDL.**
- E- HDL, VLDL, Chylomicron, LDL**

# ***Take home message***

- Because lipid compounds are relatively water insoluble, they are transported in plasma (aqueous) as Lipoproteins
- Apoproteins are the protein part of lipoproteins; they provide structural, ligand and regulatory functional for lipoprotein metabolism.
- Chylomicrons are assembled in the intestine and carry exogenous (dietary) lipids.
- Originally, chylomicrons contain only one apolipoprotein (apo B-48). Afterward, they acquire apo C-II and apo E from HDL

## SUGGESTED TEXTBOOKS



1. Lippincott's illustrated reviews in Biochemistry (6th edition) p.227-237 for cholesterol and steroid metabolism.
2. National Institutes of Health (NIH) Publication No. 01-3305 May 2001 (National Heart, Lung, and Blood Institute) Adult Treatment Panel III (ATP III) guidelines included in the National Cholesterol Education Program (NCEP) report, ATP III Guidelines At-A-Glance Quick Desk Reference.

***Thank you***

